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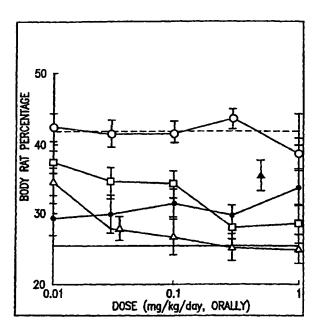
- (71) Applicant for all designated States except US): EN-DORECHERCHE, INC. [CA/CA]; 2989 de la Promenade, Ste-Foy, Quebec G1W 2J5 (CA).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): LABRIE, Fernand

[CA/CA]; 2989 de la Promenade, Ste-Foy, Quebec G1W 2J5 (CA). DESHAIES, Yves [CA/CA]; 930 rue Belvedere, St-Nicholas, Quebec G7A 3Y3 (CA). RICHARD, Denis [CA/CA]; 474 rue Fraser, Quebec City, Quebec G1S 1R4 (CA). MARTEL, Celine [CA/CA]; 1561 de Gaudarville, Ste-Foy, Quebec G2G 2H5 (CA).

- (74) Agent: MITCHELL, Richard, J.; Marks & Clerk, Station B, P.O. Box 957, Ottawa, Ontario K1P 5S7 (CA).
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(54) Title: METHODS OF TREATING AND/OR SUPPRESSING WEIGHT GAIN



(57) Abstract: Novel methods for the medical treatment and/or prevention of obesity, abdominal fat, and insulin resistance in susceptible warm-blooded animals including humans involves the administration of selective estrogen receptor modulators (SERMs). A combination of a SERM with an amount of estrogen or a sex steroid precursor selected from the group consisting of dehydroepiandrosterone, dehydroepiandrosterone sulfate, androst-5-ene-3b,17b-diol and compounds converted *in vivo* to one of the foregoing precursors or estrogen is also disclosed.



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patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, Cl, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/352 A61K31/4025 A61K31/453 A61K31/5377 A61K45/06 A61P3/04 A61P3/10 A61P3/06 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) CHEM ABS Data, MEDLINE, BIOSIS, EMBASE, SCISEARCH, EPO-Internal C. DOCUMENTS CONSIDERED TO BE RELEVANT Category ° Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. PICARD F ET AL: "Effects of the estrogen P,X 1-7,2527-35. antagonist EM - 652.HCl on energy balance 37,38 and lipid metabolism in ovariectomized INTERNATIONAL JOURNAL OF OBESITY AND RELATED METABOLIC DISORDERS, (2000 JUL) 24 (7) 830-40. XP000979846 the whole document -/--X Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: *T* later document published after the international filing date or pnority date and not in conflict with the application but cited to understand the principle or theory underlying the *A* document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another "Y" document of particular relevance; the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the document is combined with one or more other such docu-*O* document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled other means in the art *P* document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 20 February 2001 26/02/2001 Name and mailing address of the ISA Authorized officer

European Patent Office. P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Fel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

Hoff, P

Int. Ational Application No PCT/CA 00/00798

ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PCT/CA 00/00798
Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
WO 99 63974 A (ENDORECHERCHE INC) 16 December 1999 (1999-12-16)	10,11, 29-35, 37,38
abstract page 5, paragraph 4 -page 6, paragraph 1 page 23 page 34	
page 41, last paragraph -page 42, paragraph 1; examples 5,6 page 63, last paragraph -page 64, paragraph 1; claims 1,2,10,21-29,33; figure 3A	
LUO S ET AL: "COMBINED EFFECTS OF DEHYDROEPIANDROSTERONE AND EM-800 ON BONE MASS, SERUM LIPIDS, AND THE DEVELOPMENT OF DIMETHYLBENZ(A)ANTHRACENE INDUCED MAMMARY CARCINOMA IN THE RAT" ENDOCRINOLOGY, US, BALTIMORE, MD, vol. 138, no. 10, 1997, pages 4435-4444, XP000921482 ISSN: 0013-7227 the whole document	1-11, 29-35
LUO S ET AL: "PREVENTION OF DEVELOPMENT OF DIMETHYLBENZ(A)ANTHRACENE (DMBA)—INDUCED MAMMARY TUMORS IN THE RAT BY THE NEW NONSTEROIDAL ANTIESTROGEN EM-800 (SCH57050)" BREAST CANCER RESEARCH AND TREATMENT,US,NIJHOFF, BOSTON, vol. 49, no. 1, May 1998 (1998-05), pages 1-11, XP000852946 ISSN: 0167-6806 the whole document	1-7, 29-35
LABRIE F ET AL: "EM - 652 (SCH 57068), a third generation SERM acting as pure antiestrogen in the mammary gland and endometrium." JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, (1999 APR-JUN) 69 (1-6) 51-84. REF: 224, XP000852985 the whole document	10,11, 29-35, 37,38
-/	
	WO 99 63974 A (ENDORECHERCHE INC) 16 December 1999 (1999-12-16) abstract page 5, paragraph 4 -page 6, paragraph 1 page 23 page 34 page 41, last paragraph -page 42, paragraph 1; examples 5,6 page 63, last paragraph -page 64, paragraph 1; claims 1,2,10,21-29,33; figure 3A LUO S ET AL: "COMBINED EFFECTS OF DEHYDROEPIANDROSTERONE AND EM-800 ON BONE MASS, SERUM LIPIDS, AND THE DEVELOPMENT OF DIMETHYLBENZ(A)ANTHRACENE INDUCED MAMMARY CARCINOMA IN THE RAT" ENDOCRINOLOGY, US, BALTIMORE, MD, vol. 138, no. 10, 1997, pages 4435-4444, XP000921482 ISSN: 0013-7227 the whole document LUO S ET AL: "PREVENTION OF DEVELOPMENT OF DIMETHYLBENZ(A)ANTHRACENE (DMBA)- INDUCED MAMMARY TUMORS IN THE RAT BY THE NEW NONSTEROIDAL ANTIESTROGEN EM-800 (SCH57050)" BREAST CANCER RESEARCH AND TREATMENT, US, NIJHOFF, BOSTON, vol. 49, no. 1, May 1998 (1998-05), pages 1-11, XP000852946 ISSN: 0167-6806 the whole document LABRIE F ET AL: "EM - 652 (SCH 57068), a third generation SERM acting as pure antiestrogen in the mammary gland and endometrium." JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, (1999 APR-JUN) 69 (1-6) 51-84. REF: 224 XP000852985 the whole document

Int Ational Application No PCT/CA 00/00798

:/Continue	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
х	LUO S ET AL: "EFFECTS OF COMBINATION OF DEHYDROEPIAN-DROSTERONE AND EM-800 ON BONE MASS, SERUM LIPIDS, AND THE DEVELOPMENT OF DIMETHYLBENZ(A) ANTHRACENE (DMBA)-INDUCED MAMMARY CARCINOMA IN THE RAT" BREAST CANCER RESEARCH AND TREATMENT,US,NIJHOFF, BOSTON, vol. 46, no. 1, October 1997 (1997-10), page 55 XP000852947 ISSN: 0167-6806 the whole document	10,11, 29-35
X	COUILLARD S ET AL: "EFFECT OF DEHYDROEPI-ANDROSTERONE AND THE ANTIESTROGEN EM-800 ON GROWTH OF HUMAN ZR-75-1 BREAST CANCER XENOGRAFTS" JOURNAL OF THE NATIONAL CANCER INSTITUTE,US,US DEPT. OF HEALTH, EDICATIONAND WELFARE, PUBLIC HEALTH, vol. 90, no. 10, 20 May 1998 (1998-05-20), pages 772-778, XP000852955 ISSN: 0027-8874 the whole document	10,11
X	EP 0 652 006 A (LILLY CO ELI) 10 May 1995 (1995-05-10) abstract page 3, line 21 - line 35 page 7, line 51 - line 54 page 8, line 34 -page 9, line 5; claims	10,11, 37,38
X	WO 99 02152 A (NOVONORDISK AS) 21 January 1999 (1999-01-21) abstract page 3, line 1 - line 21 page 7, line 11 - line 13; claims	25
X	EP 0 635 264 A (LILLY CO ELI) 25 January 1995 (1995-01-25) abstract page 5, line 50 -page 6, line 22 page 9, line 36 - line 40; claims 1,3,4	25,27
x	WO 96 02243 A (PFIZER ;THOMPSON DAVID D (US)) 1 February 1996 (1996-02-01) cited in the application abstract; claims; example 2	12,17,18
x	WO 99 17712 A (S W PATENTVERWERTUNGS GES MBH ;SCHMIDT ALFRED (DE); WIELAND HEINRI) 15 April 1999 (1999-04-15) abstract page 7, line 24 - line 31; claims 1,13	12

Int ...tional Application No PCT/CA 00/00798

		PC1/CA 00/00/98			
C.(Continu	Bition) DOCUMENTS CONSIDERED TO BE RELEVANT				
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.			
A	WO 96 26201 A (ENDORECHERCHE) 29 August 1996 (1996-08-29) the whole document	1-38			
A		1-38			
;					

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 8,12,17,18,20,25,26,36 relate to a compound defined by reference to a desirable characteristic or property, namely "selective estrogen receptor modulator".

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to its pharmacological profile. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Furthermore, the expressions "moiety convertible in vivo to hydroxyl" and "compounds converted in vivo to any of said steroids" used in claims 1,8-11,13,20,21,24,26,27,29,36 are vague and indefinite and leave in doubt as to the meaning of the technical features (i.e. the compounds) to which they refer.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds structurally and clearly identified in the claims and examples, with due regard to the general idea underlying the present invention.

Claims searched completely: 4,7,16,19,22,23,28,32,35,37,38 Claims searched incompletely: 1-3,5,6,8-15,17,18,20,21,24-27,29,30,31,33,34,36

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

Information on patent family members

In .tional Application No PCT/CA 00/00798

Patent document cited in search report	- 1	Publication date		atent family nember(s)	Publication date
WO 9963974	A	16-12-1999	AU	4253099 A	30-12-1999
EP 0652006	A	10-05-1995	US CA JP	5446061 A 2134827 A 7215871 A	29-08-1995 06-05-1995 15-08-1995
WO 9902152	Α .	21-01-1999	AU ZA US	8433898 A 9805911 A 6016722 A	08-02-1999 11-01-1999 25-01-2000
EP 0635264	A	25-01-1995	AT AU AU CA CN CZ DE DK ES GR HU JP NO NZ PL RU US	157869 T 669627 B 6488294 A 2126400 A 1100933 A 9401520 A 69405491 D 69405491 T 635264 T 2105525 T 3025315 T 75253 A 2886453 B 7048252 A 942363 A 260790 A 303937 A 2132682 C 5567713 A	15-09-1997 13-06-1996 05-01-1995 25-12-1994 05-04-1995 15-03-1995 16-10-1997 19-02-1998 20-10-1997 27-02-1998 28-05-1997 26-04-1999 21-02-1995 27-12-1994 24-06-1997 09-01-1995 10-07-1999 22-10-1996
WO 9602243	A	01-02-1996	ZA US AU AU AU AU CA CN EP EP FI HU WO JP JP KR TW US	9404377 A 5441986 A 689257 B 2416995 A 694220 B 2417095 A 709606 B 8934898 A 2195213 A 1152868 A 0771194 A 0769941 A 1029540 A 970214 A 970215 A 77392 A 77391 A 9602242 A 9507859 T 2930424 B 9507860 T 212352 B 221854 B 403649 B 5902830 A 5827892 A	20-12-1995 15-08-1995 26-03-1998 16-02-1996 16-07-1998 16-02-1996 02-09-1999 10-12-1998 01-02-1996 01-02-1996 25-06-1997 07-05-1997 02-05-1997 23-08-2000 17-01-1997 17-01-1997 28-04-1998 28-04-1998 01-02-1996 12-08-1997 03-08-1999 12-08-1997 02-08-1999 15-09-1999 01-09-2000 11-05-1998 22-12-1998

Information on patent family members

Int .tlonal Application No PCT/CA 00/00798

Patent document cited in search report		l	Publication date	Patent family member(s)			Publication date
WO	9602243	A	<u> </u>	ZA	9505963	A	20-01-1997
		·		ZA	9505964		20-01-1997
WO	9917712	A	15-04-1999	AU	9627898		27-04-1999
				BR	9812859		08-08-2000
				EP	1021191	Α	26-07-2000
WO	9626201	Α	29-08-1996	US	6060503		09-05-2000
				AU	4660696		11-09-1996
				BR	9607259		30-12-1997
				CA	2212856		29-08-1996
				CN	1181077		06-05-1998
				EP	0811006		10-12-1997
				FI	973426		20-10-1997
				HU	9801230		28-06-1999
				JP	11500133		06-01-1999
				NO	973836		20-08-1997
				NZ	301231		28-05-1999
				PL	321892		22-12-1997
				TR	960854	A	21-10-1996
WO	9310741	Α	10-06-1993	US	5395842		07-03-1995
				AU	681338		28-08-1997
				AU	2939392		28-06-1993
				AU	4677297		19-02-1998
				CA	2124932		10-06-1993
				EP	0615448		21-09-1994
				FI	942568		27-07-1994
				JP	10273479		13-10-1998
				JP	2784846		06-08-1998
				JP	7501528		16-02-1999
				NO	942027		04-07-1994
				NZ	245339	Α	26-01-1996
				NZ	272456	Α	24-04-1997
				NZ	314240	Α	25-11-1998
				RU	2142945	С	20-12-1999
				US	5840735	Α	24-11-1998
				US	6060503	Α	09-05-2000
				US	5686465	Α	11-11-1997
				ZA	9209309	Δ	01-06-1994

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